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Published in:
Physiology & Behavior

DOI:
[10.1016/0031-9384\(88\)90186-2](https://doi.org/10.1016/0031-9384(88)90186-2)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1988

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Dantzer, R., Terlouw, C., Tazi, A., Koolhaas, J. M., Bohus, B., Koob, G. F., & Moal, M. L. (1988). The Propensity for Schedule-Induced Polydipsia is Related to Differences in Conditioned Avoidance Behaviour and in Defense Reactions in a Defeat Test. *Physiology & Behavior*, 43(3), 269-273.
[https://doi.org/10.1016/0031-9384\(88\)90186-2](https://doi.org/10.1016/0031-9384(88)90186-2)

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The Propensity for Schedule-Induced Polydipsia is Related to Differences in Conditioned Avoidance Behaviour and in Defense Reactions in a Defeat Test

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Received 16 November 1987

DANTZER, R., C. TERLOUW, A. TAZI, J. M. KOOLHAAS, B. BOHUS, G. F. KOOB AND M. LE MOAL. *The propensity for schedule-induced polydipsia is related to differences in conditioned avoidance behaviour and in defense reactions in a defeat test.* *PHYSIOL BEHAV* 43(3) 269–273, 1988.—In line with previous research showing that animals predisposed to develop schedule-induced polydipsia when submitted to intermittent distribution of food show differential behavioural and neurochemical characteristics, the present experiments investigated the nature of defense reactions to aversive situations in rats that do or do not develop schedule-induced polydipsia. It was found that rats that engage in excessive drinking during intermittent feeding display more rapid active avoidance learning in a 2-way shuttle-box and show less freezing when confronted with an aggressive resident male in a defeat test than those that do not develop schedule-induced polydipsia. These results are consistent with the hypothesis that individual differences in the propensity to exhibit oral consummatory activities in conditions of mild stress are related to the ability to shift behavioural programmes in response to external stimulation.

Adjunctive behavior	Schedule-induced polydipsia	Conditioned avoidance response
Resident-intruder paradigm	Defeat	Response stereotypy

SCHEDULE-induced polydipsia (SIP) is a form of adjunctive or displacement behaviour that occurs when food deprived rats are exposed to intermittent food schedules with simultaneous free access to water. There is still much controversy about the exact behavioural status of adjunctive behaviour [17, 18, 20, 33, 34]. However, the fact that schedule-induced polydipsia gradually develops with experience together with the observation that it leads to profound physiological consequences that cannot be attributed to the volume of water consumed have been at the source of speculations concerning the possible role of oral activities in coping with stress [3, 4, 13, 23]. More specifically, the ability to engage in drinking or other displacement activity during exposure to frustrating or conflictual situations appears to serve a buffering function by enabling the organism to reduce the activation level normally engendered by the eliciting situation. This arousal reducing function of schedule-induced polydipsia has been demonstrated in terms of

changes in plasma corticosteroid levels [9, 10, 14, 29], activation of endogenous pain inhibitory systems [30] and the locomotor response to d-amphetamine [31].

An important dimension of SIP is the existence of clear-cut individual differences in the propensity to develop this behaviour in the presence of appropriate stimulus conditions [26,30]. In exploring what factors might be responsible for these differences, animals that display excessive drinking (SIP-pos) and those that do not (SIP-neg) have been compared both within SIP sessions and in other experimental paradigms. The main result of these studies has been the observation of a consistent relationship between the propensity to respond by eating or drinking to electrical stimulation of the lateral hypothalamus (ESLH) and the predisposition to develop SIP [26]. As brain catecholamines, and specifically dopamine, have been implicated in the regulation of oral activities elicited by exposure to a wide variety of mild stressors, it has been suggested that the differences in

the predisposition to display SIP and/or ESLH-induced drinking might be related to individual differences in the responsiveness of forebrain dopamine systems [27,28]. According to this hypothesis, the predisposition to develop SIP would be another facet of a more general profile of behavioural and neurochemical reactivity to aversive situations.

One of the ways to test this possibility is to investigate whether there is any relationship between the propensity for SIP and the basic behavioural defense strategies [8] displayed in more usual aversive situations such as conditioned avoidance learning and social stress experiments. This comparison may even be of help to understand the basis of individual differences in SIP since the neurobiological mechanisms of avoidance behaviour [2] and offensive and defensive behaviour [1] are better known than those of adjunctive activities.

In the present series of experiments, we have therefore further explored the relationship between individual differences in the propensity to develop SIP and the probability to display different classes of defense reactions in a two-way avoidance procedure and in a social defeat test [22]. We found that SIP-pos rats displayed more rapid avoidance learning and froze less in response to an aggressive resident's attacks than SIP-neg rats.

METHOD

Animals

The subjects were male Sprague-Dawley rats weighing about 200 g at the start of the experiment. They were housed in individual home cages (Exp. 1) or by 4 in collective cages (Exp. 2) with water freely available, in a colony with constant temperature and humidity and a 12 hr dark/12 hr light photocycle (lights on from 7.00 a.m.).

Apparatus

The apparatus used for SIP experiments has already been fully described [29,30]. It consisted of standard operant cages without lever and with a water spout projecting into the cage at 6 cm from the food tray.

Two shuttle-boxes were used for active avoidance learning. They consisted of a two-compartment cage with a tilting floor, set inside a large soundproof box (Campden model 451). A constant current shock generator was used to deliver scrambled electric shock to the floor of the cage. Shock and warning signal (light plus high-pitched tone) were controlled by a microcomputer that also recorded on which side of the shuttle-box the animal was located.

The defeat test took place in a large wooden chamber (120×80×80 cm) with a transparent front wall. The floor of this chamber was covered with wood shavings. The chamber was located in an inverted cycle room (light on from 8.00 p.m.) and served as permanent housing for a Wistar male which was paired with a female that had undergone suture of the Fallopian tubes. The aggressiveness of the resident male was regularly checked during the dark phase of the cycle by presentation of an intruder rat, after removal of the female. Observation of the behaviour of the intruder and the resident male was carried out by means of a closed circuit video, using an infra-red sensitive camera.

Procedure

The procedure for testing of SIP has already been fully

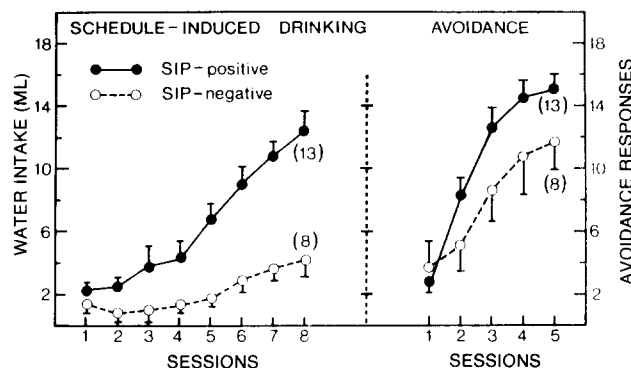


FIG. 1. Relation between schedule-induced polydipsia and avoidance learning. Left: Development of schedule-induced polydipsia in SIP-pos and SIP-neg rats. Each point represents the mean water consumption. Right: Mean number of avoidance responses per session. Vertical bars represent s.e.m.

described [29,30]. Briefly, rats maintained at approximately 85% of their free-feeding body weight were submitted to daily 30 min sessions of a fixed time 60-sec schedule of food delivery (45 mg food pellet, Bioserv) and water intake was determined by weighing the water bottle before and after each experimental session.

Experiment 1. Relation Between SIP and Avoidance Learning

After 8 sessions of SIP, 21 rats were allowed one week of free access to food before being submitted to a two-way avoidance learning. Each animal received 20 conditioning trials per day during 5 successive days. Each trial consisted of a variable 45-sec intertrial interval followed by a 5-sec warning signal. If the animal crossed the shuttle barrier during the warning signal, the trial was terminated and an avoidance was scored. If the animal failed to cross the shuttle barrier by the end of 5 sec, an electric shock was given through the floor grid. Shock and buzzer were continued until the animal escaped or for a maximum of 30 sec.

Experiment 2. Relation Between SIP and Defense Reactions in the Defeat Test

After 25 sessions of SIP, 10 rats were allowed five weeks of free access to food before being submitted to the defeat test. The same resident was used for all experimental animals that were placed individually into the home cage of the resident male for a 10 min test, after removal of the female. There were only two tests per day and the order of test was randomized in relation to the amount of water intake. From the video tapes, a trained observer unaware of the SIP status of experimental rats scored latency of the first attack and number of attacks by the resident, and number and duration of fleeing, submissive and freezing episodes displayed by the intruder. Classification of behaviour patterns in these different categories was according to Miczek [25].

RESULTS

Experiment 1. Relation Between SIP and Avoidance Learning

Figure 1A presents the mean water consumption during

TABLE 1
AGONISTIC BEHAVIOUR (MEAN \pm S.E.M.) MEASURED IN THE DEFEAT TEST

	SIP-pos Rats		SIR-neg Rats		Statistics F(1,8)
Resident					
Latency of attack	68.6 ±	11.7	72.2 ±	21.2	0.02
Number of attacks	7.4 ±	2.28	10.0 ±	1.58	0.88
Intruder					
Flight (number)	19.0 ±	7.37	22.8 ±	2.01	0.25
Flight (duration)	58.6 ±	23.2	70.2 ±	11.26	0.20
Freezing (number)	16.6 ±	7.34	22.4 ±	3.43	0.51
Freezing (duration)	67.4 ±	25.7	204.4 ±	35.5	9.77*
Submissive posture (latency)	272 ±	118	276 ±	107	0.03
Submissive posture (number)	3.0 ±	1.27	3.6 ±	1.81	0.07
Submissive posture (duration)	14.8 ±	8.25	21.2 ±	12.4	0.19

Durations are in seconds.

* $p < 0.01$.

SIP sessions. A two-way analysis of variance (2 groups \times 8 sessions) revealed that SIP-pos animals ($n=13$) drank a mean amount of 6.52 ml water per session whereas SIP-neg rats ($n=8$) drank only 2.15 ml. This difference was highly significant, $F(1,19)=24.8, p < 0.01$. In addition, the amount of water ingested varied across sessions, $F(7,133)=34.0, p < 0.01$, but this variation was not the same in SIP-pos and in SIP-neg rats [interaction group \times session, $F(7,133)=9.62, p < 0.01$]. Post hoc analysis of group means with the least significant difference test revealed that SIP-pos animals drank more water than SIP-neg animals from the third session on.

Figure 1B presents the mean number of avoidance responses during the 5 sessions of avoidance learning. A two-way analysis of variance (2 groups \times 5 sessions) showed a near-significant group factor, $F(1,19)=3.07, p < 0.10$, a significant session factor, $F(4,76)=43.3, p < 0.01$, and a significant group \times session interaction, $F(4,76)=2.60, p < 0.05$. Post hoc analysis of group means with the least significant difference test revealed that SIP-pos rats emitted a higher number of avoidance responses than SIP-neg rats from the second session on. In addition, there was a significant correlation between the mean amount of water consumed over the 8 days of SIP testing and the mean number of avoidance responses over the 5 days of avoidance conditioning (Spearman rank correlation: $r=.56, p < 0.05$).

Experiment 2. Relation Between SIP and Defense Reactions in the Defeat Test

During the last session of SIP testing, SIP-pos animals ($n=5$) drank from 16 to 21 ml water (mean $=19 \pm 1.1$ ml) whereas SIP-neg animals drank only 2–5 ml (mean: 3.5 ± 0.9 ml). This difference is highly significant.

Table 1 presents the incidence and duration of agonistic behaviours of the resident and the intruder during the defeat test. Typically, placement of the intruder into the resident's cage induced approach and sniffing of the intruder by the resident. This was followed by attacks from the resident male, that took place within approximately one minute from

the start of the test. In response to attacks or after them, the intruder usually adopted a defensive posture that differed according to the resident's behaviour and proximity. Flight or submissive posture usually occurred during the course of a flight while freezing (an immobile crouch posture) took place after a fight when the dominant was at some distance, or before a fight, during grooming by the resident rat. The major difference between SIP-pos and SIP-neg rats was the shorter duration of freezing displayed by the former animals, $F(1,8)=9.77, p = 0.01$, in spite of a similar pattern of attack by the resident male.

DISCUSSION

The present results demonstrate that rats that differ in their predisposition to drink during intermittent distribution of food also differ in the rate of avoidance learning and the extent of freezing they display when confronted with an aggressive resident male.

There is already some evidence suggesting that the propensity to develop SIP is associated to a more general predisposition to engage in oral displacement activities in a number of experimental situations [13, 26, 32]. However, up to now, there has been no attempt to relate these differences to possible differences in basic behavioural defense reactions to aversive situations. Confronted with potential threat, rats are known to engage primarily in flight, fight or freezing. Selection between these strategies depends on the relative hierarchy of these responses in the animals' repertoire and their effectiveness in enabling the subject to cope with eliciting situation [8].

Large inter-individual differences are commonly found in behavioural responses to aversive situations. In the case of active avoidance, these individual differences have not been systematically studied, with the noticeable exception of the Roman strains. These strains were originally selected by Bignami [6] out of a population of Wistar rats on the basis of their speed of acquisition and retention of conditioned avoidance responding in a standard 2-way shuttle-box. Al-

though these strains have mainly been studied for their emotionality and learning abilities [15], there is evidence that the Roman High Avoiders (RHA) more easily develop schedule-induced ethanol polydipsia than the Roman Low Avoiders (RLA) [24]. The neurochemical mechanisms responsible for the differential acquisition of the two-way active avoidance response by RHA and RLA rats have remained remarkably elusive in spite of several intensive studies [15,16]. In view of the involvement of dopamine in conditioned avoidance responding, it is noteworthy that treatment with d-amphetamine has been found to consistently facilitate avoidance behaviour in RLA rats [11].

Significant individual differences in aggression during social interactions have also been reported in the resident-intruder paradigm [22]. Aggressive males differed from non-aggressive males not only in the resident-intruder situation, but also in a number of other situations such as active avoidance and maze learning [5,7]. Aggressive animals developed stereotyped routines whereas the behaviour of non-aggressive individuals was more flexible, and depended upon interaction with external cues. These animals also differed in their reactions when placed as intruders into the cage of a resident male (defeat test). Aggressive males responded mainly by defense or escape (fleeing) whereas non-aggressive males mainly displayed freezing. On the basis of an extensive series of neuropharmacological investigations, those animals that primarily froze in the defeat test were found to have a relatively high mesolimbic noradrenergic activity and a high neostriatal dopaminergic activity [12]. In contrast, animals that primarily fled had a low mesolimbic noradrenergic activity and a low neostriatal dopaminergic activity.

Taken together with the results of the present experiment, these data converge to suggest that the predisposition to develop SIP is a facet of a more general profile of behavioural and neurochemical reactivity, that may be related to brain dopaminergic systems [27,28]. The basic factor underlying the differences between SIP-pos and SIP-neg animals may be

the ability to shift behavioural programmes, i.e., behavioural flexibility [12]. Typically, SIP-neg rats are individuals that engage in some drinking but remain flexible in their behaviour and do not develop routines. In contrast, SIP-pos rats become more and more stereotyped in their drinking patterns as they develop the behaviour [20]. In the same way, RHA rats are described as more stereotyped and less flexible than RLA rats in several types of testing situations [15]. Furthermore, rats that have a low mesolimbic noradrenergic activity together with a low neostriatal dopamine activity are claimed to be "stimulus-bound," i.e., they are less able than rats with high mesolimbic noradrenergic activity and high neostriatal dopamine activity to select arbitrarily behavioural strategies [12]. The same concept has recently been postulated by King [21] to account for the relation between mesolimbic dopamine and temperament.

In conclusion, the results of the present experiments suggest that the predisposition to develop SIP during exposure to an intermittent distribution of food is part of a more complex profile of behavioural and neurochemical reactivity that is associated with characteristic patterns of defensive reactions to other aversive situations and may involve brain dopaminergic systems. It is not yet known whether these differences preexist to the SIP experience and are revealed by it, or whether they are merely consecutive to the SIP experience. In addition, the exact nature of the behavioural and neurochemical mechanisms of these differences remains to be elucidated.

ACKNOWLEDGEMENTS

Part of this work (Exp. 1) was carried out in Bordeaux thanks to a grant to C.T. from the Commission of the European Communities' Concerted Action on Quantification of Parameters for the Study of Breakdown in Human Adaptation. The other part of the work (Exp. 2) took place in San Diego and this was supported in part by NIH grant AM26741 and the MacArthur Foundation (G.F.K. and A.T.). Many thanks are due to Dr. A. Cools for stimulating discussion.

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